REMARKS

Claim Amendments

Claim 1 has been amended to recite "expanding" rather than "culturing".

Claims 13 and 16 have been amended to depend from claim 1, only. This amendment to claim 16 necessitated further addition of the limitations from claim 15 into claim 16.

Claims 2-8 have been amended to recite "[T]he process according to claim 1…"

Claim 3 is cancelled and the limitations of claim 3 are incorporated into claim 1.

The dependencies of claim 4-6 have been amended to recite claim 1, instead of claim 3.

A period has been added to the end of claim 9.

Claim 11 has been amended to recite a mesenchymal progenitor cell composition.

Claim Rejections – 35 USC § 112

The Examiner rejected claims 13 and 16 as being in improper multiple dependent form. These claims have been amended to depend from claim 1, only.

The Examiner rejected claims 2-8 as being indefinite. These claims have been amended to recite "[T]he process according to claim 1…"

Claim Rejections – 35 USC § 102

Baksh *et al.*

The Examiner rejected claims 1-3 and 8-16 as being anticipated by Baksh *et al.* (WO 02/086104A1). The Examiner asserted that claim 1 was anticipated by Baksh *et al.* because claim 1 was not directed to a method of growing progenitor cells in a medium that is serum-deprived medium and under non-static conditions (para. 13).

In response, the Applicant has amended claim 1 to recite that the method is one for expanding progenitor cells. Hence, the claim as amended is directed to a method of expanding progenitor cells, which method is accomplished by culturing the cells in a medium that is serum-deprived and under non-static conditions. This method is not taught by Baksh *et al.*

The instant application is directed to a serum free culture system for "expanding" progenitor cells – see for example the Abstract. The terms "expand(s, ed, ing, able)", "expansion", are used well over 100 times in the application.

The term "expanding" is not defined in the application because it is a term of common usage, which means to increase in the number of cells over time, in culture. See for example the enclosure from "*A Code of Practice for the Production of Human-derived Therapeutic Products*, which defines "cell expansion" as "increasing the quantity of cells by their replication *in vitro*."

A review of the specification indicates that this is how the term "expand" is used in the specification. Enclosed is the specification in which all instances of the use of the word "expand" (or a variant thereof) are underlined. As shown, when read in plain context, the word "expand" can only refer to an increase in cell number. The term is used consistently and frequently in accord with its common usage.

Several times in the specification there is a reference to an increase total cell number, which is the measure used to determine whether expansion has occurred or not. And, in a several instances, expand is equated with "proliferate", which means to multiply.

There are several instances where an explicit mention is made of total cell number, or total CFU formed, as being the relevant factor in determining whether or not there has been "expansion" - for example page 5, lines 13 to 18; pg. 15, lines 9 to 12 and lines 14 to 24; pg. 16, lines 22-24; pg. 17, lines 24-26; pg. 21, lines 23-30.

The Experimental data, which is used to demonstrate the expansion of cells, also supports that this term relates to "number of cells", as Figures 1, 3, and 4 measure the

number of cells or CFUs produced under various culture conditions. Thus, providing support that "expansion" has been achieved. The use of the term “expanding” in claim 1 is fully supported by the specification.

Baksh *et al.* teaches that serum-free medium is used for differentiation of progenitors into chondroblasts, not for expansion of cells.

The Examiner asserts that the statement in Baksh *et al.* at para. [0079] that “[f]or differentiation into chondroblasts, the progenitors can be grown in serum-free DMEM supplemented with TGF-beta” means that the person of skill in the art would understand that the progenitors are *grown* in serum-free medium (paragraph 18 of Office Action). The Applicant respectfully disagrees.

As explained by the declaration of Dr. Baksh, submitted with the previous response, this text describes an assay for differentiating progenitors into chondrocytes [pg. 3, Baksh Declaration]. The fact that the text in paragraph [0079] states that the medium is supplemented with TGF-beta, which is an inducer of differentiation, clearly indicates that the cells are being differentiated.

Further, Dr. Baksh addresses directly the Examiner’s assertion that this passage describes growing progenitor cells in serum-free medium. Dr. Baksh states: “This is not correct, either. The stem and/or progenitor cells do not actually grow; they only differentiate” [pg. 4, 2nd para., Baksh Declaration]. Thus, the Applicant has provided a declaration which explains that a person of skill in the art would understand this statement to mean that the progenitors are differentiated in serum-free medium, not grown in serum free medium. This is not what is claimed in claim 1, as amended.

The Examiner asserts that a person of skill in the art would interpret the term “suspension” as used in para. 0079 to refer to suspension cultures that are stirred (paragraph 16 of Office Action). The Applicant respectfully disagrees. Baksh *et al.* generally relates to a novel and inventive method of expanding human progenitor cells by suspension culturing under non-static conditions. Paragraphs [0094] to [0098], referred to by the Examiner in paragraph 16 refer to the methods used to “expand” progenitor cells.

When it comes to discussing differentiation, and not expansion, Baksh *et al.* teaches in paragraph [0078] that the progenitor cells are induced to differentiate "using techniques established in the art". Paragraph [0079] immediately follows and discusses differentiation of progenitors into chondroblasts, which would be understood to be accomplished "using techniques established in the art". Because Baksh *et al.* relates to a method of expanding human progenitor cells by suspension culturing under non-static conditions, the term "techniques established in the art" as used in paragraph [0078] would be understood to mean static suspension cultures. Thus, paragraph [0079] does indeed relate to static suspension cultures.

For both of these reasons, the Applicant submits that claims 1-3 and 8-16, as amended, are novel over Baksh *et al.*

Kallos *et al.*

The Examiner rejected claims 1-2, 7-8, 11 and 13-15 as being anticipated by Kallos *et al.* (2003), which relates to neural stem cell culture methods. In response, the Applicant has amended claim 1 to incorporate the limitation of claim 3, rendering the objection moot. Further, claim 11 has been amended to recite a mesenchymal progenitor cell composition.

Claim Rejections – 35 USC § 103

The Examiner rejected claims 1-16 as being obvious by Baksh *et al.* (WO 02/086104A1) in view of Cancedda *et al.* (US 6,617,159). The Examiner asserts that Cancedda *et al.* discloses the use of anchorage-independent culturing conditions for expanding mesenchymal cells. The Examiner points to the claims of Cancedda *et al.* in support of this proposition.

The Applicant submits that there is nothing in Cancedda *et al.* that teaches, or that would even suggest, that growing of the mesenchymal cells was done using anchorage-independent culturing conditions. Quite to the contrary, each of the Examples 1-3, which teach how to grow mesenchymal cells, do so in anchorage-dependent conditions (col. 3, lines 39-40; col. 4, lines 26-28 and col. 4, line 67 to col. 5, line 1). To *induce differentiation* mesenchymal cells were grown in anchorage-independent conditions

(Example 4, col. 5, lines 24-26). Thus a person of skill in the art reading Cancedda *et al.* would understand and expect that growing mesenchymal cells in anchorage-independent conditions in serum-free medium would actually induce differentiation, which is not the result obtained using the non-static culturing methods of the present application.

The Examiner relies on an interpretation of the *claims* of Cancedda *et al.* which is broader than and unsupported by the *teachings* of Cancedda *et al.,* to argue that Cancedda *et al.* teaches that the serum-free medium can be used for growing mesenchymal progenitor cells in anchorage-independent conditions. This is clearly not what Cancedda *et al.* teaches, and goes beyond the disclosure of this reference.

Therefore, the Applicant submits that claims 1-16 are not obvious when Baksh *et al.* (WO 02/086104A1) is combined with Cancedda *et al.* (US 6,617,159).

In view of the foregoing, the Applicant submits that the application is in condition for allowance, and requests that the Examiner withdraw the rejection against all claims and allow all claims.

Favourable consideration is respectfully requested.

Respectfully submitted,
HEENAN BLAIKIE LLP

By: /Susan Rancourt/
Susan Rancourt, Ph.D.
Reg. No. 56,016

Bay Adelaide Centre
333 Bay Street, Suite 2900
P.O. Box 2900
CANADA M5H 2T4
(416) 643-6813